REMARKS

Status of Claims

Claims 29-32 have been newly added. Thus, claims 1-32 are now pending. Claims 1-19 and 22 were withdrawn from consideration by the Examiner as being drawn to a nonelected invention. Claims 20, 21 and 23-32 are under consideration.

Amendments to the Claims

Claims 25 and 27 have been amended to remove the recitation of soluble CD40 ligand (sCD40L). These claim amendments do not add any new matter. New claims 29-32 have been added in order to create separate claims for methods for determining the prognosis of acute cardiovascular disease (claims 29-30) and for diagnosing acute cardiovascular disease (claims 31-32) comprising determining the concentration of sCD40L and at least one additional selected marker. The subject matter of new claims 29-30 was encompassed by previous claim 25, and the subject matter of new claims 31-32 was encompassed by previous claim 27. None of the new claims therefore adds any new matter. Furthermore, the new claims all fall within the elected Group III ("drawn to therapeutic methods monitoring acute cardiovascular diseases;" *see* Office Action mailed June 10, 2009, at page 3).

Withdrawal of Rejections of Record

Applicants acknowledge with thanks the withdrawal of the rejections of record upon the Office's consideration of Applicants' amendment and response. *See* Office Action, page 4.

Finality of the Office Action

Applicants respectfully disagree with the finality of the Office Action. The Office presented new grounds of rejection in this Office Action and argued that Applicants' amendment filed on June 25, 2010, necessitated the new grounds of rejection and that accordingly the Office Action is properly made final. *See* Office Action at page 4. Applicants disagree that the current rejections were necessitated by the amendments made on June 25, 2010, because these amendments merely created separate claims for the methods for diagnosis, prognosis, and therapy monitoring, which were previously all encompassed in a single claim (see previous claim 20). The amended claims filed on June 25, 2010, do not encompass any subject matter that was not already encompassed by the previous claims. Therefore, the amendments cannot have necessitated the new rejections which are based on the newly cited reference of Schönbeck et al.. Applicants thus believe that the finality of the Office Action is premature and request that the Office reconsider and withdraw the finality of the Office Action. *See* M.P.E.P. § 706.07(d).

Rejections under 35 U.S.C. §102 - Novelty Requirement

Claims 25-28 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Schönbeck et al. (Circulation, Vol. 104, pages 2266-2268 (2001)) ("Schönbeck"). Office Action, pages 2-3. According to the Office, Schönbeck discloses methods of measuring soluble CD40L (sCD40L) in patients with unstable angina, based on the observation that the immune-signaling dyad CD40/CD40L promotes atherogenesis and is elevated in patients with unstable angina. *Id.* at page 2. The Office further contends that sCD40L levels of healthy middle-age women were found to

be significantly higher in participants who subsequently (in a 4 year follow-up) developed myocardial infarction, stroke, and cardiovascular death. *Id.* at page 3. Applicants respectfully traverse for the following reasons.

As a consequence of the claim amendments, currently pending claims 25-26 are directed to a method for determining the prognosis of acute cardiovascular disease comprising determining the concentration of at least one inflammatory marker selected from PAPP-A and PlGF. Furthermore, currently pending claims 27-28 are directed to a method for diagnosing acute cardiovascular disease comprising determining the concentration of PlGF. The amended claims 25-28 no longer encompass methods comprising determining the concentration of sCD40L. Thus, the rejections are moot with respect to amended claims 25-28.

New claims 29-32 are directed to methods for determining the prognosis of acute cardiovascular disease (claims 29-30) and for diagnosing acute cardiovascular disease (claims 31-32) comprising determining the concentrations of sCD40L and of at least one additional marker selected from the markers provided in subpart (c) of claims 29 and 31. Thus, the methods of new claims 29-32 require the measurement of sCD40L and of at least one additional marker. Schönbeck does not teach, neither expressly nor inherently, any method that requires the measurement of at least one marker in addition to the measurement of sCD40L. However, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); M.P.E.P. § 2131. Thus, because Schönbeck does not teach every element of new claims 29 and 31, it cannot anticipate these

claims. Because new claims 30 and 32 depend from claims 29 and 31, respectively, Schönbeck also cannot anticipate claims 30 and 32.

Applicants therefore respectfully submit that amended claims 25-28 and new claims 29-32 are not anticipated by Schönbeck and request withdrawal of the rejection under 35 U.S.C. §102(b).

Rejections under 35 U.S.C. §103 - Nonobviousness Requirement

Claims 20, 21, 23 and 24 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Schönbeck in view of Corsini et al. (Pharmacology & Therapeutics 84:413-428 (1999)) ("Corsini"). Office Action, pages 3-4. The Office acknowledges that Schönbeck does not specifically teach the administration of statins as a therapeutic vascular agent to a patient. *Id.* at page 3. The Office contends, however, that Corsini teaches procedures for administering statins to patients and the effects of statins in ameliorating vascular atherosclerosis and reducing cardiovascular-related morbidity and mortality in patients. *Id.* at page 4. The Office concludes that it would have been obvious to one of skill in the art to treat the detected vascular patients of Schönbeck with the statins of Corsini. *Id.* Applicants respectfully traverse for the following reasons.

Claims 20, 21, 23 and 24 are directed to the monitoring of therapy of acute cardiovascular disease. In the context of the present invention, "monitoring of the therapy" relates to controlling and, optionally, adjusting the therapeutic treatment for an individual. The "therapeutic treatment" includes any treatment that possibly improves the pathophysiological condition of an individual, including, for example, the administration of pharmaceutical agents (e.g. the glycoprotein IIb/IIIa-inhibitor

abciximab) as well as surgical or physically invasive treatment (e.g. balloon dilatation) (*see, e.g.*, specification at page 15, 1st ¶).

Markers that are useful for diagnosing a disease or for identifying apparently healthy individuals at risk of developing a disease do not necessarily allow controlling or adjusting the therapeutic treatment of a patient with the disease and thus are not necessarily useful for monitoring of the therapy of that disease. The instant specification teaches, based on experimental evidence, that the therapeutic treatment of a patient can be controlled or adjusted according to the status of certain markers, such as sCD40L, PAPP-A and PlGF (*see, e.g.*, specification at Examples, pages 29 to 54). Schönbeck does not teach or suggest using any of these inflammatory markers for the monitoring of therapy of acute cardiovascular disease. Furthermore, Corsini does not make up for this deficiency of Schönbeck. The alleged teaching by Corsini of procedures for administering statins to patients and the effects of statins in ameliorating vascular atherosclerosis and reducing cardiovascular-related morbidity and mortality in patients does not make it obvious to one of skill in the art to use at least one of the inflammatory markers sCD40L, PAPP-A and PlGF for the monitoring of therapy of acute cardiovascular disease, even if the therapy comprises the administration of statins. The teachings of Corsini relate to the nature of a therapy, such as the administration of statins, but not to a method for monitoring a therapy as understood in the instant invention. Even if therapy of acute cardiovascular disease with administration of statins would have been obvious to one of ordinary skill in the art, this would not have made it obvious to one of ordinary skill in the art that this therapy can be monitored, i.e.

controlled and, optionally, adjusted, by a method comprising determining the concentration of sCD40L, PAPP-A and/or PlGF.

In summary, neither Schönbeck nor Corsini, nor the combination of both, provide any teaching or suggestion that determining the concentration of sCD40L, PAPP-A and/or PlGF could be used for monitoring the therapy of acute cardiovascular disease, even if this therapy includes the administration of statins. One of ordinary skill in the art would therefore have no good reason or motivation to attempt using sCD40L, PAPP-A and/or PlGF for this purpose. Furthermore, one of ordinary skill in the art would have no reasonable expectation of success in using any of these three markers for monitoring a therapy of acute cardiovascular disease, and using any of these three markers for this purpose would not yield predictable results.

Based on the Supreme Court's decision in *KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 1734 (2007), the Office has formulated exemplary rationales that may support a conclusion of obviousness. *See* M.P.E.P. § 2143. All of these rationales for obviousness require that one of ordinary skill in the art, without knowing anything of the claimed invention, would not only have a good reason or motivation to produce that invention, but also would have a reasonable expectation of success or achieve predictable results. Since these requirements are not met in the instant case, Applicants submit that claims 20, 21, 23 and 24 are not obvious over Schönbeck in view of Corsini.

Whether Corsini actually teaches procedures for administering statins to patients and the effects of statins in ameliorating vascular atherosclerosis and reducing

cardiovascular-related morbidity and mortality in patients, as contended by the Office, does not change this conclusion.

In view of the above, Applicants respectfully request that the rejection of claims 20, 21, 23 and 24 under 35 U.S.C. § 103(a) be withdrawn.

Conclusion

In view of the foregoing remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims. If the Examiner believes a telephone conference would be useful in resolving any outstanding issues, the Examiner is invited to call the undersigned at (202) 408-4316.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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By: 
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